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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/550,331	02/22/2007	Adrienne S. Gordon	12101-013-999	2103

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EXAMINER	
CORNET, JEAN P	
ART UNIT	PAPER NUMBER
1628	
MAIL DATE	DELIVERY MODE
11/13/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/550,331	GORDON ET AL.	
	Examiner	Art Unit	
	JEAN CORNET	1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 August 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1, 21, 36, 58, 78, 86, 93, 95, 118, 119, 134, 137, 142,1 145-* is/are pending in the application.

4a) Of the above claim(s) *21,36,58,78,86,93,95,118,119,134,137,142 and 145* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 146-163* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *07/20/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of Group I, claim 1 and newly added claims 146-163 in the reply filed on 08/20/2009 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

1. Claims 1, 21, 36, 58, 78, 86, 93, 95, 118, 119, 134, 137, 142, and 145-are currently pending. Claims 2-20, 22-35, 37-57, 59-77, 79-85, 87-92, 94, 96-117, 120-133, 138-141, 143-144, are canceled by Applicant. Claims 21, 36, 58, 78, 86, 93, 95, 118, 119, 134, 137, 142, and 145 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 1, 146-163 are currently under examination.

Priority

2. Applicant's claim foreign priority to benefit to PCT/US2003/009629, filed on 03/27/2003, which claims priority to Provisional application 60/368417, filed on 03/27/2002 is acknowledged.

Information Disclosure Statement

3. All references submitted on the IDS dated 07/20/2009 and 09/16/2009 have been considered except the pending applications where no copies were provided. All the pending applications cited in the IDS will be considered if the corresponding PG Pubs are provided.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim1, 146-163 are rejected under 35 U.S.C. 103(a) as being unpatentable over Diamond et al (US5,069,895) in view of Yao et al ($\beta\gamma$ Dimers mediate synergy of dopamine D2 and adenosine A2 receptor-stimulated PKA signaling and regulate ethanol consumption) and Beasley et al. (US6,159,963).

The invention is directed to a method of mitigating one or more symptoms associated with chronic consumption of a substance abuse by a mammal comprising administering to said mammal an effective amount of an adenosine receptor antagonist and an effective amount of a dopamine receptor antagonist.

Diamond teaches methods of treating acute, chronic ethanol dependence or withdrawal syndrome by administration of adenosine A2 receptor antagonist to a host in an amount sufficient to reduce the symptoms of ethanol withdrawal (see claim 1 and 11). Although the standard therapeutically effective dosage for use is generally in the range from about 0.01ug/kg to 5 mg/kg as to claim 150, the amount will depend on the subject being treated, the severity and nature of the affliction, the manner of administration, the potency and pharmacodynamics of the particular agent (col. 5, ln. 11-19). The preferred adenosine antagonist is PD115,199 (col. 3, lines 7-30)

Diamond does not expressly teach administration of a dopamine D2 receptor to treat ethanol addictive behavior.

Yao discloses that dopamine D2 receptors are involved in a cellular signaling mechanism tied with adenosine A2 receptors, which leads to D2 and A2 synergy, see abstract. With respect to claims Yao also discloses neurons expressing both D2 and A2 are uniquely sensitive to low or sub-threshold concentrations of ethanol in the presence of dopamine and drugs that target synergy of adenosine and dopamine receptors will prevent, attenuate or reverse excessive drinking (right col., second paragraph).

Beasley teaches a method for treating substance abuse comprising administering an effective amount of olanzapine (a dopamine antagonist) to a patient in need thereof (abstract) and a method for treating adverse withdrawal syndrome said substance abuse include opiods, cocaine, anxiolytic and hypnotic drugs, and alcohol (col. 1, lines 65-67; col, 2, lines 1-3) and adverse withdrawal syndrome refers to an adverse condition resulting form the cessation or withdrawal from substance abuse (col. 5, lines 25-28). For the treatment of alcohol abuse, a lower dosage may be appropriate than treatment than the preferred standard effective dose of 1mg to 25mg per day (col 7, lines 35-45).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the reference and to mitigate on or more symptoms associated with chronic consumption of a substance abuse by administration of adenosine receptor antagonist and dopamine receptor antagonist . One or ordinary skill in the art would have been motivated to do so because the beneficial synergistic effect of adenosine A2 and dopamine D2 receptors has been fully disclosed at the time of filling.

As to the limitation "wherein the effective amount of adenosine receptor antagonist is lower than the effective amount of an adenosine receptor antagonist…." of claim 1 and 146 It is the purview of one skilled in the art to reduce the amount of active agents when combining two agents to reduce side affect and toxicity and improve patient compliance.

With respect to claims 147 and 160, one skill in the art would have been motivated to administer the combined D2 and A2 antagonists sequentially to produce minimum activation of PKA in response to consumption of a substance abuse because each of the therapeutics agents with an effective dose had been individually taught in the prior art to be successful at treating substance abuse. The instant situation is amenable to the type of analysis set forth *in re Kerkhoven*, 205 USPQ 1069 (CCPA 1980) wherein the court held that it is prima facie obvious to combine two compositions that is taught by the prior art to be useful for the same purpose in order for a third composition that is to be used for the very same purpose since the idea of combining them flows logically from their having been individually taught in the prior art. Applying the same logic to the instant process claims, one of ordinary skill in the art would have had reasonable expectation of success that by administering an effective dose of adenosine receptor antagonist taught Diamond et al in combination with an effective dose of dopamine receptor antagonist taught by Beasley et al, one would achieve a method of treating one or more symptoms associated with chronic consumption of a substance abuse.

With respect to claim161 and 162, the synergy of the A2 and D2 antagonists as suggested by Yao meet this limitation of claim 161. As to claim 160, one of ordinary skill would have recognized to formulate a single unit dose to reduce number of drugs a patient would have to take and to improve patient's compliance by enhancing patient satisfaction whereas the technique and skill required for making that formulation is well within conventional knowledge.

With respect to claims 148-152, even though the references are silent as to administration of a standard, sub-threshold, and a threshold dosage, It would have been prima facie obvious to one of ordinary skill in the art to combine the teaching of Diamond and Beasley to optimize via routine experimentation the dosage range recited in Diamond and Beasley because Diamond suggests the amount PD 115,199 depends on the subject being treated, the severity and nature of the affliction, the manner of administration, the potency and pharmacodynamics of the particular agent and Beasly suggest a lower dose than the standard dose for the treatment of alcohol, thus resulting in the practice of the instantly claimed invention.

MPEP 2144.5(A) states:

Optimization Within Prior Art Conditions or Through Routine Experimentation

> Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955)

One would have been motivated to do so; with reasonable expectation of success because such optimization is routine in the pharmaceutical and would have

been readily accomplished by one of ordinary skill in the art without undue burden. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

With respect to claims 155, 156, 158, 159, one would have recognized lowering the dosage of these agents would reduce the side effects caused by these agents. The side effect recited in these claims is well known because these compounds are well known in the art and efficacy and toxicity have already been proven. These minor differences found adverse symptoms does not render the claims patentable distinct because the techniques and skills for determining efficacy and toxicity are well within the level of the ordinary skilled artisan and commonly practiced in the stat of the art, and thus absent evidence to the contrary.

Double Patenting

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 153, 154, 157, 160-163 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 4, 6, 19-24 of copending Application No. 11/153,725. Although the conflicting claims are not identical, they are not patentably distinct from each other because the scope of the instant claimed subject matter, method of mitigating one or more symptoms associated with chronic consumption of a substance abuse by a mammal by administration of an adenosine receptor antagonist and .a dopamine receptor antagonist is fully covered by the subject matter of the copending application in claims 1, 4, 6, 19-24, method of mitigating a component of addiction behavior associated with chronic consumption of a substance of abuse or withdrawal therefrom, by a mammal by administration of an adenosine A2 receptor antagonist and further comprises administering a dopamine D2 receptor antagonist in claim 19.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

7. No claims allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JEAN CORNET whose telephone number is (571)270-7669. The examiner can normally be reached on Monday-Thursday 7.00am-5.30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brandon Fetterolf can be reached on 571-272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/JC/

/Brandon J Fetterolf/
Primary Examiner, Art Unit 1642